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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/779,447	02/09/2001	Dipak K. Banerjee	P19850.p06	6690

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EXAMINER	
OWENS JR, HOWARD V	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 05/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/779,447	BANERJEE ET AL.	
	Examiner	Art Unit	
	Howard V Owens	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *9/12/2001* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Arguments

The following is in response to the amendment filed 3/12/04:

An action on the merits of claims 2-18 is contained herein below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Finality of the last office action is withdrawn.

Claim for Domestic Priority

The claim for domestic priority under 35 U.S.C. 119(e) to provisional application no. 60/181,312 is acknowledged.

Request for Approval of Drawing Corrections

The drawings were received on September 12, 2001. These drawings are approved.

Response to Restriction Requirement

Applicant's election with traverse of Group I in Paper No. 11 is acknowledged. It is noted that Groups I-III have been acted on by the examiner and thus comments regarding the examination of these groups for restriction purposes are moot. The traversal for groups IV - XIV is on the ground(s) that an appropriate explanation of how a serious burden would be imposed has not been stated by the examiner. This is not found persuasive because as cited in the restriction requirement mailed 1/6/03, "these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper. To search fourteen distinct and divergent inventions would impose an undue burden upon an examiner assigned this application". Thus an explanation of why an undue burden would be imposed was set forth;

moreover, applicant has not responded as to how the examiner was in err with respect to the distinct and divergent classification of the inventions set forth in Groups IV-XIV.

This application contains claims drawn to an invention nonelected with traverse in Paper No. 11. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. The requirement is still deemed proper and is therefore made **FINAL**.

35 U.S.C. 103

Applicant's arguments filed 3/12/04 have been fully considered but they are not persuasive.

The rejection of claims 2-18 under 35 U.S.C. 103 as being unpatentable over Banerjee et al., *Indian J. Biochem. and Biophysics*, vol. 30(6), pp. 389-94 and Tiganis et al., *Exp. Cell Research*, vol. 198, pp. 191-200 (1992) is maintained for the reasons of record..

Claims 2-14 and 16-18 are drawn to a method for inhibiting angiogenesis comprising administering a pyrimidine nucleoside, wherein the nucleoside comprises N-acetylated glucosamine or comprises tunicamycin and functional derivatives thereof.

Claim 15 is drawn to the method of claim 1, wherein the inhibition of angiogenesis occurs in a variety of diseases wherein inhibition of angiogenesis would be beneficial, i.e. diabetic retinopathy, artherosclerotic plaques, schleroderma, etc.

Banerjee teaches that angiogenesis comprises (1)endothelial cell proliferation and (2) differentiation into blood capillaries. Banerjee teaches the use of a pyrimidine nucleoside as an antiangiogenic agent as it teaches that the angiogenic process of capillary endothelial cell proliferation is linked to the synthesis of N-linked oligosaccharide chains which is inhibited by the pyrimidine nucleoside tunicamycin (which contains a linked glucosamine). Tiganis et al., further supports the recognition in the prior art of the inhibition of N-glycosylation by tunicamycin and the disruption of vascular proliferation or angiogenesis. Tiganis teaches that the inhibition of glycoproteins by tunicamycin impairs the cell adhesion and the functional properties of

the endothelial lining of the blood vessels. Thus one of skill in the art would have a reasonable expectation of success that if Tunicamycin is a potent inhibitor of N-glycosylation and that this inhibition disrupts component (1) of angiogenesis, there is clearly a reasonable expectation of success in the use of tunicamycin as an agent which would inhibit angiogenesis.

Aside from presenting new arguments, applicant should note that there has been no specific response by applicant to the discussion of homologs set forth in the prior office action with regards to the Banerjee reference. As cited in the specific office action Banerjee does not specifically mention the claimed homologs of tunicamycin nor the various diseases wherein angiogenesis may be present ; however, characteristics normally possessed by members of a homologous series are principally the same, chemists would in general know what to expect in adjacent members of homologs of a known compound. The test of patentability of a compound that is a homologue of a prior art compound is whether the claimed compound possesses beneficial characteristics which are unexpected and unobvious. One of skill in the art would have a reasonable expectation of success in the use of homologs of tunicamycin as angiogenic compounds given the efficacy of the parent compound. There is not data in the prior art nor the specification that presents some property of these homologs apart from that of the parent compound, chiefly the inhibition of angiogenesis. One of skill in the art would also have a reasonable expectation of success that a compound which inhibits angiogenesis would be beneficial in various disease states which may be disrupted by or thrive on the process of angiogenesis. Applicant's claims regarding the administration timetable of the know compound is not patentable given that one of skill in the art practicing the administration of any medical compound determines the optimum dosage for each patient, based on a variety of physical and metabolic factors.

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to use a pyrimidine nucleoside such as tunicamycin to inhibit angiogenesis.

A person of ordinary skill in the art would have been motivated to use a pyrimidine nucleoside such as tunicamycin given the prior art's recognition of tunicamycin as an

inhibitor of the pathway leading to the angiogenic process of capillary endothelial cell proliferation.

Applicant argues that Banerjee does not teach or suggest inhibiting angiogenesis using a nucleoside comprising glucosamine or a nucleoside comprising a pyrimidine nucleoside let alone tunicamycin and functional derivatives thereof; moreover that Banerjee is chiefly concerned with the evaluation of isoproterenol and it's mediation of protein glycosylation.

It should be noted that applicant has not responded to the specific citations in the reference showing Tunicamycin as an inhibitor of N-glycosylation; moreover, applicant would contend that because the aim of the study was not Tunicamycin, any teachings presented in the reference showing Tunicamycin as an inhibitor of N-glycosylation are not relevant. As cited in the previous office action, applicant should note that tunicamycin is a glucosamine containing nucleoside compound (emphasis added). Banerjee teaches that protein N-glycosylation and angiogenesis are indeed interlinked (p.293, ¶ 3); moreover, that Tunicamycin inhibited N-glycosylation in control cells by 64% and those treated with isoproterenol by 70% (p. 392, col.1-col.2). Thus Banerjee has recognized that Tunicamycin is a potent N-glycosylation inhibitor, as such given the teachings by Banerjee that angiogenesis is linked to N-glycosylation, one of skill in the art would have a reasonable expectation of success in the use of Tunicamycin to inhibit angiogenesis. Moreover, as cited supra, Tiganis et al., further supports the recognition in the prior art of the inhibition of N-glycosylation by tunicamycin and the disruption of vascular proliferation or angiogenesis.

The teachings of Tiganis verify that Tunicamycin is a potent inhibitor of glycoprotein synthesis in endothelial cells (see Discussion, p. 198) as equally purported by the teachings of Banerjee. As cited supra, Banerjee teaches that angiogenesis is a two part process, endothelial cell proliferation and differentiation. Clearly, one of skill in the art presented with the teachings of Tiganis on the ability of Tunicamycin to inhibit the proliferation of endothelial cells would find sufficient motivation in the use of Tunicamycin for the disruption or inhibition of angiogenesis.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Howard V. Owens
Patent Examiner
Art Unit 1623

Samuel Barts
Primary Patent Examiner
Technology Center 1600

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (703) 306-4538 . The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent Examiner signing this action, James O. Wilson can be reached on (703) 308-4624 . The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.